EAST Search History

Ref #	Hits	Search Query	DBs	Default Operator	Plurals	Time Stamp
S1	1405	tetrahydrocannabinol	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2006/09/26 13:15
S2	8230	glioblastoma	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2006/09/26 13:15
S3	36	S1 S2	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	AND	OFF	2006/09/26 13:15
S4	5	"4189491"	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	AND	OFF	2006/09/26 13:16
S5	5	"6,939,429"	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	AND	OFF	2006/09/26 13:16

=> **file medline, caplus, wpids**

=> **s glioblastoma?**
L1 20535 GLIOBLASTOMA?

=> **s tetrahydrocannibol**
L2 6 TETRAHYDROCANNIBOL

=> **s tetrahydrocannibinol**
L3 79 TETRAHYDROCANNIBINOL

=> **s tetrahydrocannabinol**
L4 10433 TETRAHYDROCANNABINOL

=> **s l4 and l1**
L5 14 L4 AND L1

=> **d l5 1-14 ibib, abs**

L5 ANSWER 1 OF 14 MEDLINE on STN
ACCESSION NUMBER: 2006412347 IN-PROCESS Full-text
DOCUMENT NUMBER: PubMed ID: 16804518
TITLE: A pilot clinical study of Delta9-tetrahydrocannabinol in patients with recurrent glioblastoma multiforme.
AUTHOR: Guzman M; Duarte M J; Blazquez C; Ravina J; Rosa M C; Galve-Roperh I; Sanchez C; Velasco G; Gonzalez-Feria L
CORPORATE SOURCE: Department of Biochemistry and Molecular Biology I, School of Biology, Complutense University, Madrid 28040, Spain.. mgp@bbm1.ucm.es
SOURCE: British journal of cancer, (2006 Jul 17) Vol. 95, No. 2, pp. 197-203. Electronic Publication: 2006-06-27. Journal code: 0370635. ISSN: 0007-0920.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: NONMEDLINE; IN-PROCESS; NONINDEXED; Priority Journals
ENTRY DATE: Entered STN: 13 Jul 2006
Last Updated on STN: 4 Aug 2006

AB Delta(9)-Tetrahydrocannabinol (THC) and other cannabinoids inhibit tumour growth and angiogenesis in animal models, so their potential application as antitumoral drugs has been suggested. However, the antitumoral effect of cannabinoids has never been tested in humans. Here we report the first clinical study aimed at assessing cannabinoid antitumoral action, specifically a pilot phase I trial in which nine patients with recurrent glioblastoma multiforme were administered THC intratumoraly. The patients had previously failed standard therapy (surgery and radiotherapy) and had clear evidence of tumour progression. The primary end point of the study was to determine the safety of intracranial THC administration. We also evaluated THC action on the length of survival and various tumour-cell parameters. A dose escalation regimen for THC administration was assessed. Cannabinoid delivery was safe and could be achieved without overt psychoactive effects. Median survival of the cohort from the beginning of cannabinoid administration was 24 weeks (95% confidence interval: 15-33). Delta(9)- Tetrahydrocannabinol inhibited tumour-cell proliferation in vitro and decreased tumour-cell Ki67 immunostaining when administered to two patients. The fair safety profile of THC, together with its possible antiproliferative action on tumour cells reported here and in other studies, may set the basis for future trials aimed at evaluating the potential antitumoral activity of cannabinoids.

L5 ANSWER 2 OF 14 MEDLINE on STN
ACCESSION NUMBER: 2006209507 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 16616335
TITLE: The stress-regulated protein p8 mediates cannabinoid-induced apoptosis of tumor cells.
AUTHOR: Carracedo Arkaitz; Lorente Mar; Egia Ainara; Blazquez Cristina; Garcia Stephane; Giroux Valentin; Malicet Cedric; Villuendas Raquel; Gironella Meritxell; Gonzalez-Feria Luis; Piris Miguel Angel; Iovanna Juan L; Guzman Manuel; Velasco Guillermo
CORPORATE SOURCE: Department of Biochemistry and Molecular Biology I, School of Biology, Complutense University, 28040 Madrid, Spain.
SOURCE: Cancer cell, (2006 Apr) Vol. 9, No. 4, pp. 301-12.
Journal code: 101130617. ISSN: 1535-6108.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200605
ENTRY DATE: Entered STN: 18 Apr 2006
Last Updated on STN: 17 May 2006
Entered Medline: 16 May 2006

AB One of the most exciting areas of current research in the cannabinoid field is the study of the potential application of these compounds as antitumoral drugs. Here, we describe the signaling pathway that mediates cannabinoid-induced apoptosis of tumor cells. By using a wide array of experimental approaches, we identify the stress-regulated protein p8 (also designated as candidate of metastasis 1) as an essential mediator of cannabinoid antitumoral action and show that p8 upregulation is dependent on de novo-synthesized ceramide. We also observe that p8 mediates its apoptotic effect via upregulation of the endoplasmic reticulum stress-related genes ATF-4, CHOP, and TRB3. Activation of this pathway may constitute a potential therapeutic strategy for inhibiting tumor growth.

L5 ANSWER 3 OF 14 MEDLINE on STN
ACCESSION NUMBER: 2005413320 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 16078104
TITLE: Cannabinoids selectively inhibit proliferation and induce death of cultured human glioblastoma multiforme cells.
AUTHOR: McAllister Sean D; Chan Calvin; Taft Ryan J; Luu Tri; Abood Mary E; Moore Dan H; Aldape Ken; Yount Garret
CORPORATE SOURCE: California Pacific Medical Center Research Institute, 475 Brannan St., Suite 220, San Francisco, CA 94107, USA.. mcallis@sutterhealth.org
CONTRACT NUMBER: 05274 (NCCAM)
09978
AT00643
SOURCE: Journal of neuro-oncology, (2005 Aug) Vol. 74, No. 1, pp. 31-40.
Journal code: 8309335. ISSN: 0167-594X.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200510
ENTRY DATE: Entered STN: 4 Aug 2005
Last Updated on STN: 15 Oct 2005

Entered Medline: 14 Oct 2005

AB Normal tissue toxicity limits the efficacy of current treatment modalities for glioblastoma multiforme (GBM). We evaluated the influence of cannabinoids on cell proliferation, death, and morphology of human GBM cell lines and in primary human glial cultures, the normal cells from which GBM tumors arise. The influence of a plant derived cannabinoid agonist, Delta(9)-tetrahydrocannabinol Delta(9)-THC), and a potent synthetic cannabinoid agonist, WIN 55,212-2, were compared using time lapse microscopy. We discovered that Delta(9)-THC decreases cell proliferation and increases cell death of human GBM cells more rapidly than WIN 55,212-2. Delta(9)-THC was also more potent at inhibiting the proliferation of GBM cells compared to WIN 55,212-2. The effects of Delta(9)-THC and WIN 55,212-2 on the GBM cells were partially the result of cannabinoid receptor activation. The same concentration of Delta(9)-THC that significantly inhibits proliferation and increases death of human GBM cells has no significant impact on human primary glial cultures. Evidence of selective efficacy with WIN 55,212-2 was also observed but the selectivity was less profound, and the synthetic agonist produced a greater disruption of normal cell morphology compared to Delta(9)-THC.

L5 ANSWER 4 OF 14 MEDLINE on STN

ACCESSION NUMBER: 2004408103 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 15313899
TITLE: Cannabinoids inhibit the vascular endothelial growth factor pathway in gliomas.
AUTHOR: Blazquez Cristina; Gonzalez-Feria Luis; Alvarez Luis; Haro Amador; Casanova M Llanos; Guzman Manuel
CORPORATE SOURCE: Department of Biochemistry and Molecular Biology I, School of Biology, Complutense University, Madrid, Spain.
SOURCE: Cancer research, (2004 Aug 15) Vol. 64, No. 16, pp. 5617-23.
Journal code: 2984705R. ISSN: 0008-5472.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200409
ENTRY DATE: Entered STN: 18 Aug 2004
Last Updated on STN: 1 Oct 2004
Entered Medline: 30 Sep 2004

AB Cannabinoids inhibit tumor angiogenesis in mice, but the mechanism of their antiangiogenic action is still unknown. Because the vascular endothelial growth factor (VEGF) pathway plays a critical role in tumor angiogenesis, here we studied whether cannabinoids affect it. As a first approach, cDNA array analysis showed that cannabinoid administration to mice bearing s.c. gliomas lowered the expression of various VEGF pathway-related genes. The use of other methods (ELISA, Western blotting, and confocal microscopy) provided additional evidence that cannabinoids depressed the VEGF pathway by decreasing the production of VEGF and the activation of VEGF receptor (VEGFR)-2, the most prominent VEGF receptor, in cultured glioma cells and in mouse gliomas. Cannabinoid-induced inhibition of VEGF production and VEGFR-2 activation was abrogated both in vitro and in vivo by pharmacological blockade of ceramide biosynthesis. These changes in the VEGF pathway were paralleled by changes in tumor size. Moreover, intratumoral administration of the cannabinoid Delta9-tetrahydrocannabinol to two patients with glioblastoma multiforme (grade IV astrocytoma) decreased VEGF levels and VEGFR-2 activation in the tumors. Because blockade of the VEGF pathway constitutes one of the most promising antitumoral approaches currently available, the present findings provide a novel pharmacological target for cannabinoid-based therapies.

L5 ANSWER 5 OF 14 MEDLINE on STN
ACCESSION NUMBER: 2004133485 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 15026328
TITLE: Cannabinoids induce cancer cell proliferation via tumor necrosis factor alpha-converting enzyme (TACE/ADAM17)-mediated transactivation of the epidermal growth factor receptor.
AUTHOR: Hart Stefan; Fischer Oliver M; Ullrich Axel
CORPORATE SOURCE: Department of Molecular Biology, Max-Planck-Institute of Biochemistry, Am Klopferspitz 18A, D-82152 Martinsried, Germany.
SOURCE: Cancer research, (2004 Mar 15) Vol. 64, No. 6, pp. 1943-50.
Journal code: 2984705R. ISSN: 0008-5472.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200404
ENTRY DATE: Entered STN: 18 Mar 2004
Last Updated on STN: 9 Apr 2004
Entered Medline: 8 Apr 2004

AB Cannabinoids, the active components of marijuana and their endogenous counterparts were reported as useful analgetic agents to accompany primary cancer treatment by preventing nausea, vomiting, and pain and by stimulating appetite. Moreover, they have been shown to inhibit cell growth and to induce apoptosis in tumor cells. Here, we demonstrate that anandamide, Delta(9)-tetrahydrocannabinol (THC), HU-210, and Win55,212-2 promote mitogenic kinase signaling in cancer cells. Treatment of the glioblastoma cell line U373-MG and the lung carcinoma cell line NCI-H292 with nanomolar concentrations of THC led to accelerated cell proliferation that was completely dependent on metalloprotease and epidermal growth factor receptor (EGFR) activity. EGFR signal transactivation was identified as the mechanistic link between cannabinoid receptors and the activation of the mitogen-activated protein kinases extracellular signal-regulated kinase 1/2 as well as prosurvival protein kinase B (Akt/PKB) signaling. Depending on the cellular context, signal cross-communication was mediated by shedding of proAmphiregulin (proAR) and/or proHeparin-binding epidermal growth factor-like growth factor (proHB-EGF) by tumor necrosis factor alpha converting enzyme (TACE/ADAM17). Taken together, our data show that concentrations of THC comparable with those detected in the serum of patients after THC administration accelerate proliferation of cancer cells instead of apoptosis and thereby contribute to cancer progression in patients.

L5 ANSWER 6 OF 14 MEDLINE on STN
ACCESSION NUMBER: 2001080899 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 11108795
TITLE: Serum-dependent effects of tamoxifen and cannabinoids upon C6 glioma cell viability.
AUTHOR: Jacobsson S O; Rongard E; Stridh M; Tiger G; Fowler C J
CORPORATE SOURCE: Department of Pharmacology and Clinical Neuroscience, Umea University, SE-901 87, Umea, Sweden.
SOURCE: Biochemical pharmacology, (2000 Dec 15) Vol. 60, No. 12, pp. 1807-13.
Journal code: 0101032. ISSN: 0006-2952.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English

FILE SEGMENT: Priority Journals
ENTRY MONTH: 200101
ENTRY DATE: Entered STN: 22 Mar 2001
Last Updated on STN: 22 Mar 2001
Entered Medline: 11 Jan 2001

AB In the present study, the effects of the combination of tamoxifen ((Z)-2[p-(1,2-diphenyl-1-butenyl)phenoxy]-N,N-dimethylamine citrate) and three cannabinoids (Delta(9)-tetrahydrocannabinol [Delta(9)-THC], cannabidiol, and anandamide [AEA]) upon the viability of C6 rat glioma cells was assessed at different incubation times and using different culturing concentrations of foetal bovine serum (FBS). Consistent with previous data for human glioblastoma cells, the tamoxifen sensitivity of the cells was increased as the FBS content of the culture medium was reduced from 10 to 0.4 and 0%. The cells expressed protein kinase C alpha and calmodulin (the concentration of which did not change significantly as the FBS concentration was reduced), but did not express estrogen receptors. Delta(9)-THC and cannabidiol, but not AEA, produced a modest reduction in cell viability after 6 days of incubation in serum-free medium, whereas no effects were seen in 10% FBS-containing medium. There was no observed synergy between the effects of tamoxifen and the cannabinoids upon cell viability.

L5 ANSWER 7 OF 14 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2006:692024 CAPLUS Full-text
TITLE: A pilot clinical study of Δ9-tetrahydrocannabinol in patients with recurrent glioblastoma multiforme
AUTHOR(S): Guzman, M.; Duarte, M. J.; Blazquez, C.; Ravina, J.; Rosa, M. C.; Galve-Roperh, I.; Sanchez, C.; Velasco, G.; Gonzalez-Feria, L.
CORPORATE SOURCE: Department of Biochemistry and Molecular Biology I, School of Biology, Complutense University, Madrid, 28040, Spain
SOURCE: British Journal of Cancer (2006), 95(2), 197-203
CODEN: BJCAAI; ISSN: 0007-0920
PUBLISHER: Nature Publishing Group
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Δ9-Tetrahydrocannabinol (THC) and other cannabinoids inhibit tumor growth and angiogenesis in animal models, so their potential application as antitumoral drugs has been suggested. However, the antitumoral effect of cannabinoids has never been tested in humans. Here we report the first clin. study aimed at assessing cannabinoid antitumoral action, specifically a pilot phase I trial in which nine patients with recurrent glioblastoma multiforme were administered THC intratumoraly. The patients had previously failed standard therapy (surgery and radiotherapy) and had clear evidence of tumor progression. The primary end point of the study was to determine the safety of intracranial THC administration. We also evaluated THC action on the length of survival and various tumor-cell parameters. A dose escalation regimen for THC administration was assessed. Cannabinoid delivery was safe and could be achieved without overt psychoactive effects. Median survival of the cohort from the beginning of cannabinoid administration was 24 wk (95% confidence interval: 15-33). Δ9-Tetrahydrocannabinol inhibited tumor-cell proliferation in vitro and decreased tumor-cell Ki67 immunostaining when administered to two patients. The fair safety profile of THC, together with its possible antiproliferative action on tumor cells reported here and in other studies, may set the basis for future trials aimed at evaluating the potential antitumoral activity of cannabinoids.

L5 ANSWER 8 OF 14 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2006:393185 CAPLUS Full-text
DOCUMENT NUMBER: 144:404250
TITLE: The stress-regulated protein p8 mediates cannabinoid-induced apoptosis of tumor cells
AUTHOR(S): Carracedo, Arkaitz; Lorente, Mar; Egia, Ainara; Blazquez, Cristina; Garcia, Stephane; Giroux, Valentin; Malicet, Cedric; Villuendas, Raquel; Gironella, Meritxell; Gonzalez-Feria, Luis; Piris, Miguel Angel; Iovanna, Juan L.; Guzman, Manuel; Velasco, Guillermo
CORPORATE SOURCE: Department of Biochemistry and Molecular Biology I, School of Biology, Complutense University, Madrid, 28040, Spain
SOURCE: Cancer Cell (2006), 9(4), 301-312
CODEN: CCAECI; ISSN: 1535-6108
PUBLISHER: Cell Press
DOCUMENT TYPE: Journal
LANGUAGE: English
AB One of the most exciting areas of current research in the cannabinoid field is the study of the potential application of these compds. as antitumoral drugs. Here, we describe the signaling pathway that mediates cannabinoid-induced apoptosis of tumor cells. By using a wide array of exptl. approaches, we identify the stress-regulated protein p8 (also designated as candidate of metastasis 1) as an essential mediator of cannabinoid antitumoral action and show that p8 upregulation is dependent on de novo-synthesized ceramide. We also observe that p8 mediates its apoptotic effect via upregulation of the endoplasmic reticulum stress-related genes ATF-4, CHOP, and TRB3. Activation of this pathway may constitute a potential therapeutic strategy for inhibiting tumor growth.
REFERENCE COUNT: 47 THERE ARE 47 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 9 OF 14 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:1303230 CAPLUS Full-text
DOCUMENT NUMBER: 144:304660
TITLE: Cannabinoids selectively inhibit proliferation and induce death of cultured human glioblastoma multiforme cells
AUTHOR(S): McAllister, Sean D.; Chan, Calvin; Taft, Ryan J.; Luu, Tri; Abood, Mary E.; Moore, Dan H.; Aldape, Ken; Yount, Garret
CORPORATE SOURCE: California Pacific Medical Center Research Institute, San Francisco, CA, USA
SOURCE: Journal of Neuro-Oncology (2005), 74(1), 31-40
CODEN: JNODD2; ISSN: 0167-594X
PUBLISHER: Springer
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Normal tissue toxicity limits the efficacy of current treatment modalities for glioblastoma multiforme (GBM). We evaluated the influence of cannabinoids on cell proliferation, death, and morphol. of human GBM cell lines and in primary human glial cultures, the normal cells from which GBM tumors arise. The influence of a plant derived cannabinoid agonist, Δ9-tetrahydrocannabinol (Δ9-THC), and a potent synthetic cannabinoid agonist, WIN 55,212-2, were compared using time lapse microscopy. We discovered that Δ9-THC decreases cell proliferation and increases cell death of human GBM cells more rapidly than WIN 55,212-2. Δ9-THC was also more potent at inhibiting the proliferation of

GBM cells compared to WIN 55,212-2. The effects of Δ9-THC and WIN 55,212-2 on the GBM cells were partially the result of cannabinoid receptor activation. The same concentration of Δ9-THC that significantly inhibits proliferation and increases death of human GBM cells has no significant impact on human primary glial cultures. Evidence of selective efficacy with WIN 55,212-2 was also observed but the selectivity was less profound, and the synthetic agonist produced a greater disruption of normal cell morphol. compared to Δ9-THC.

REFERENCE COUNT: 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 10 OF 14 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:812059 CAPLUS Full-text
DOCUMENT NUMBER: 142:127351
TITLE: Arachidonylethanolamide induces apoptosis of human glioma cells through vanilloid receptor-1
AUTHOR(S): Contassot, Emmanuel; Wilmotte, Rick; Tenan, Mirna; Belkouch, Marie-Claude; Schnuriger, Valerie; de Tribolet, Nicolas; Bourkhardt, Karim; Dietrich, Pierre-Yves
CORPORATE SOURCE: Laboratory of Tumor Immunology, University Hospital, Geneva, Switz.
SOURCE: Journal of Neuropathology and Experimental Neurology (2004), 63(9), 956-963
CODEN: JNENAD; ISSN: 0022-3069
PUBLISHER: American Association of Neuropathologists, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The anti-tumor properties of cannabinoids have recently been evidenced, mainly with Δ9-tetrahydrocannabinol (THC). However, the clin. application of this drug is limited by possible undesirable side effects due to a broad expression of cannabinoid receptors (CB1 and CB2). An attractive field of research therefore is to identify mols. with more selective tumor targeting. This is particularly important for malignant gliomas, considering their poor prognosis and their location in the brain. Here we investigated whether the most potent endogenous cannabinoid, arachidonylethanolamide (AEA), could be a candidate. We observed that AEA induced apoptosis in long-term and recently established glioma cell lines via aberrantly expressed vanilloid receptor-1 (VR1). In contrast with their role in THC-mediated death, both CB1 and CB2 partially protected glioma against AEA-induced apoptosis. These data show that the selective targeting of VR1 by AEA or more stable analogs is an attractive research area for the treatment of glioma.

REFERENCE COUNT: 56 THERE ARE 56 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 11 OF 14 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:672684 CAPLUS Full-text
DOCUMENT NUMBER: 141:218491
TITLE: Cannabinoids Inhibit the Vascular Endothelial Growth Factor Pathway in Gliomas
AUTHOR(S): Blazquez, Cristina; Gonzalez-Feria, Luis; Alvarez, Luis; Haro, Amador; Casanova, M. Llanos; Guzman, Manuel
CORPORATE SOURCE: Department of Biochemistry and Molecular Biology I, School of Biology, Complutense Univ., Madrid, Spain
SOURCE: Cancer Research (2004), 64(16), 5617-5623
CODEN: CNREA8; ISSN: 0008-5472
PUBLISHER: American Association for Cancer Research
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Cannabinoids inhibit tumor angiogenesis in mice, but the mechanism of their antiangiogenic action is still unknown. Because the vascular endothelial growth factor (VEGF) pathway plays a critical role in tumor angiogenesis, here the authors studied whether cannabinoids affect it. As a first approach, cDNA array anal. showed that cannabinoid administration to mice bearing s.c. gliomas lowered the expression of various VEGF pathway-related genes. The use of other methods (ELISA, Western blotting, and confocal microscopy) provided addnl. evidence that cannabinoids depressed the VEGF pathway by decreasing the production of VEGF and the activation of VEGF receptor (VEGFR)-2, the most prominent VEGF receptor, in cultured glioma cells and in mouse gliomas. Cannabinoid-induced inhibition of VEGF production and VEGFR-2 activation was abrogated both in vitro and in vivo by pharmacol. blockade of ceramide biosynthesis. These changes in the VEGF pathway were paralleled by changes in tumor size. Moreover, intratumoral administration of the cannabinoid Δ9-tetrahydrocannabinol to two patients with glioblastoma multiforme (grade IV astrocytoma) decreased VEGF levels and VEGFR-2 activation in the tumors. Because blockade of the VEGF pathway constitutes one of the most promising antitumoral approaches currently available, the present findings provide a novel pharmacol. target for cannabinoid-based therapies.

REFERENCE COUNT: 53 THERE ARE 53 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 12 OF 14 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2004:214360 CAPLUS Full-text

DOCUMENT NUMBER: 140:350165

TITLE: Cannabinoids Induce Cancer Cell Proliferation via Tumor Necrosis Factor α-Converting Enzyme (TACE/ADAM17)-Mediated Transactivation of the Epidermal Growth Factor Receptor

AUTHOR(S): Hart, Stefan; Fischer, Oliver M.; Ullrich, Axel

CORPORATE SOURCE: Department of Molecular Biology, Max-Planck-Institute of Biochemistry, Martinsried, Germany

SOURCE: Cancer Research (2004), 64(6), 1943-1950
CODEN: CNREA8; ISSN: 0008-5472

PUBLISHER: American Association for Cancer Research

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Cannabinoids, the active components of marijuana and their endogenous counterparts were reported as useful analgetic agents to accompany primary cancer treatment by preventing nausea, vomiting, and pain and by stimulating appetite. Moreover, they have been shown to inhibit cell growth and to induce apoptosis in tumor cells. Here, we demonstrate that anandamide, Δ9-tetrahydrocannabinol (THC), HU-210, and Win55212-2 promote mitogenic kinase signaling in cancer cells. Treatment of the glioblastoma cell line U373-MG and the lung carcinoma cell line NCI-H292 with nanomolar concns. of THC led to accelerated cell proliferation that was completely dependent on metalloprotease and epidermal growth factor receptor (EGFR) activity. EGFR signal transactivation was identified as the mechanistic link between cannabinoid receptors and the activation of the mitogen-activated protein kinases extracellular signal-regulated kinase 1/2 as well as prosurvival protein kinase B (Akt/PKB) signaling. Depending on the cellular context, signal cross-communication was mediated by shedding of proAmphiregulin (proAR) and/or proHeparin-binding epidermal growth factor-like growth factor (proHB-EGF) by tumor necrosis factor α converting enzyme (TACE/ADAM17). Taken together, our data show that concns. of THC comparable with those detected in the serum of patients after THC administration accelerate proliferation of cancer cells instead of apoptosis and thereby contribute to cancer progression in patients.

REFERENCE COUNT: 42 THERE ARE 42 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 13 OF 14 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2000:854152 CAPLUS Full-text
DOCUMENT NUMBER: 134:231621
TITLE: Serum-dependent effects of tamoxifen and cannabinoids upon C6 glioma cell viability
AUTHOR(S): Jacobsson, S. O. P.; Rongard, E.; Stridh, M.; Tiger, G.; Fowler, C. J.
CORPORATE SOURCE: Department of Pharmacology and Clinical Neuroscience, Umea University, Umea, SE-901 87, Swed.
SOURCE: Biochemical Pharmacology (2000), 60(12), 1807-1813 December
CODEN: BCPCA6; ISSN: 0006-2952
PUBLISHER: Elsevier Science Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB In the present study, the effects of the combination of tamoxifen ((Z)-2[p-(1,2-diphenyl-1-butenyl)phenoxy]-N,N-dimethylamine citrate) and three cannabinoids (Δ9-tetrahydrocannabinol [Δ9-THC], cannabidiol, and anandamide [AEA]) upon the viability of C6 rat glioma cells was assessed at different incubation times and using different culturing concns. of fetal bovine serum (FBS). Consistent with previous data for human glioblastoma cells, the tamoxifen sensitivity of the cells was increased as the FBS content of the culture medium was reduced from 10 to 0.4 and 0%. The cells expressed protein kinase C α and calmodulin (the concentration of which did not change significantly as the FBS concentration was reduced), but did not express estrogen receptors. Δ9-THC and cannabidiol, but not AEA, produced a modest reduction in cell viability after 6 days of incubation in serum-free medium, whereas no effects were seen in 10% FBS-containing medium. There was no observed synergy between the effects of tamoxifen and the cannabinoids upon cell viability.
REFERENCE COUNT: 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 14 OF 14 WPIDS COPYRIGHT 2006 THE THOMSON CORP on STN
ACCESSION NUMBER: 2001-536502 [59] WPIDS
DOC. NO. CPI: C2001-159728
TITLE: Use of natural or synthetic cannabinoid compounds for treating brain tumors, particularly glioblastoma , without side effects.
DERWENT CLASS: B02
INVENTOR(S): GALVE, R I; GUZMAN, P M; SANCHEZ, G C; GALVE ROPERH, I; GUZMAN PASTOR, M; SANCHEZ GARCIA, C
PATENT ASSIGNEE(S): (UYMA-N) UNIV COMPLUTENSE MADRID; (ROPE-I) GALVE ROPERH I; (PAST-I) GUZMAN PASTOR M; (GARC-I) SANCHEZ GARCIA C
COUNTRY COUNT: 30
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2001058445	A1	20010816	(200159)*	ES	24
RW: AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE TR					
W: AU BR CA CN JP MX NO NZ SG US					
AU 2001013979	A	20010820	(200175)		
EP 1177790	A1	20020206	(200218)	EN	
R: AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE TR					
ES 2164584	A1	20020216	(200223)		
US 2004039048	A1	20040226	(200416)		
EP 1177790	B1	20050511	(200536)	EN	

R: AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE TR
DE 60020111 E 20050616 (200540)
ES 2241670 T3 20051101 (200577)
DE 60020111 T2 20060309 (200622)

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2001058445	A1	WO 2000-ES450	20001122
AU 2001013979	A	AU 2001-13979	20001122
EP 1177790	A1	EP 2000-976087	20001122
		WO 2000-ES450	20001122
ES 2164584	A1	ES 2000-323	20000211
US 2004039048	A1 Div ex	WO 2000-ES450	20001122
	Div ex	US 2001-958960	20011127
		US 2003-647739	20030825
EP 1177790	B1	EP 2000-976087	20001122
		WO 2000-ES450	20001122
DE 60020111	E	DE 2000-00020111	20001122
		EP 2000-976087	20001122
		WO 2000-ES450	20001122
ES 2241670	T3	EP 2000-976087	20001122
DE 60020111	T2	DE 2000-00020111	20001122
		EP 2000-976087	20001122
		WO 2000-ES450	20001122

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 2001013979	A	Based on	WO 2001058445
EP 1177790	A1	Based on	WO 2001058445
EP 1177790	B1	Based on	WO 2001058445
DE 60020111	E	Based on	EP 1177790
		Based on	WO 2001058445
ES 2241670	T3	Based on	EP 1177790
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PRIORITY APPLN. INFO: ES 2000-323 20000211
AN 2001-536502 [59] WPIDS
AB WO 200158445 A UPAB: 20011012
NOVELTY - Use of natural or synthetic cannabinoids (I) to prepare a composition for treating, in mammals (including humans) a wide range of brain tumors.

DETAILED DESCRIPTION - Use of natural or synthetic cannabinoids (I) to prepare a composition for treating, in mammals (including humans) a wide range of brain tumors. Tumors that can be treated include glioblastoma, meduloepithelioma, medulоblastoma, neuroblastoma, germinoma, embryonal or plexal carcinoma, astrocytoma, astroblastoma, ependimoma, oligodendroglioma, neuroepithelioma, pineoblastoma, ependimoblastoma, neuroectodermal tumors, malignant meningioma, chondrosarcoma, meningeal sarcomatosoma, malignant melanoma or malignant schwannoma.

ACTIVITY - Antitumor. 5 million C6 glioblastoma cells were implanted into the fronto-parietal lobe of the right cerebral hemisphere in rats. Starting 12 days after implantation (when mean tumor volume was 70 cubic mm), the synthetic cannabinoid WIN-55212-2 was administered through a cannula, inserted at the implantation site. Treatment was over 7 days and the total dose (depending on characteristics of the tumor) was 50-250 micro g. Mean survival

times were significantly longer than for controls and complete eradication of the tumor was achieved in 5 of the 15 cases.

MECHANISM OF ACTION - Selective agonism of cannabinoid receptors causes selective killing of transformed cells.

USE - (I) are used to treat a wide range of brain tumors, especially glioblastoma.

ADVANTAGE - Brain tumors can be regressed (or even eradicated) without significant side-effects, by a simple and effective treatment. Dwg.0/0

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